No. 17-290

IN THE

Supreme Court of the United States

MERCK SHARP & DOHME CORP.,

Petitioner,

v.

DORIS ALBRECHT, ET AL.,

Respondents.

On Writ of Certiorari
To The United States Court of Appeals
For The Third Circuit

REPLY BRIEF FOR PETITIONER

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INTRODUCTION

Respondents do not dispute that Merck shared the available scientific data with the FDA, proposed to warn about the risk of "low-energy femoral shaft fracture[s]," and was rebuffed by the FDA in a formal written response. Yet Respondents insist that Merck may be held liable for failure to warn under state tort law, because a jury might conclude—after holding Merck to an unjustifiably heightened burden of proof—that the FDA chose to keep doctors and patients in the dark about a genuine safety risk simply because it did not like Merck's choice of *terminology* for the type of fracture.

The law forecloses that speculation. Instead, it presumes that the FDA properly discharges its duties, including its statutory obligation to work with manufacturers on labeling changes when it becomes aware of new safety information. The FDA's conscious choice not to do so when confronted with a proposed revision and the relevant data thus establishes, as a matter of law, that the manufacturer could not have changed its label to comply with state law's purported demands.

Merck should still prevail even if the law allows courts to second-guess the FDA as Respondents insist. The FDA has now told this Court that it would not have allowed Merck to add a warning before September 2010, and that comports with every other known fact. There could hardly be any "clear[er] evidence that the FDA would not have approved" the changes state law demanded, *Wyeth v. Levine*, 555 U.S. 555, 571 (2009), particularly under the *ordinary* burden of proof.

ARGUMENT

I. THE FDA'S DENIAL OF MERCK'S PROPOSED WARNING PREEMPTS RESPONDENTS' CLAIMS AS A MATTER OF LAW.

Merck's argument is simple: When a drug manufacturer proposes warning about a risk and shares all the relevant scientific data, but the FDA responds with a "no," the manufacturer cannot be held liable for failure to warn about that risk. That is because the FDA's actual rejection legally establishes the impossibility of adding a warning. Any other conclusion ignores the FDA's statutory obligations and its own regulatory framework—as now confirmed by the United States. Respondents dispute this legal rule and deny that it applies here; they are wrong in both respects.

A. Failure-To-Warn Claims Are Preempted When the FDA Rejects a Proposed Warning About a Disclosed Risk.

All parties agree that if the FDA prevented or "would have prevented" a drug manufacturer "from adding a stronger warning," state-law claims based on a failure to do so are preempted. *Levine*, 555 U.S. at 573; *see* Resp. Br. 30. The question is how to prove that condition. Merck's point is that, as a matter of law, the agency "would have prevented" a warning if, after being informed of the relevant risk, the agency prevented a proposed warning about it.

This follows from the governing statutory and regulatory regime. When the FDA "becomes aware of new safety information"—including information provided by a manufacturer—"that [it] determines should be included in the labeling," the FDA "*shall*

promptly notify" the manufacturer, seek a response, and then "promptly review and act upon" that response. 21 U.S.C. § 355(*o*)(4)(A)–(C) (emphasis added). And under FDA regulations, a proposed labeling change may be rejected only if it is deficient in substance, not just in semantics. *See* 21 C.F.R. § 314.102(b) (FDA must make "every reasonable effort" to communicate "easily correctable deficiencies"); *id.* § 314.105(b) (if a proposal's "only deficiencies ... concern editorial or similar minor deficiencies in the draft labeling," FDA will conditionally approve). The FDA interprets these rules the same way. *See* U.S. Br. 32–33.

Given the presumption of regularity afforded to the FDA's conduct, the agency's informed decision to reject a proposal shows that it did not believe the risk justified a warning. Otherwise, it would have honored its obligations under § 355(*o*)(4) and worked with the manufacturer toward mutually acceptable revisions. Similarly, it would have honored its own regulatory promise to smooth over "editorial or similar minor deficiencies in the draft labeling," such as by suggesting alternative language. If it did not do so, and instead rejected the proposal, the law permits only one conclusion: The FDA did not permit the manufacturer to warn about the risk in question, and thus, at that time, would not have permitted any new warning about that risk. In other words, it would have been impossible to warn about the relevant risk without contradicting the FDA, in violation of federal law. The FDA does not put patient health and informed consent in jeopardy by rejecting scientifically justified warnings simply

because it disagrees with a manufacturer's proposed phrasing. Again, the FDA agrees. U.S. Br. 31–33.

This rule makes good sense. Because all agree that determining the meaning and effect of the FDA's complete response letter is a question for the court, this rule avoids the specter of numerous juries deploying their "intuitions" about "administrative inertia and agency decision-making processes" to decide preemption. Pet.App.54a. It also places the relevant burdens on the right shoulders. Manufacturers, for their part, must monitor scientific developments and seek a label change if necessary. But the FDA retains the final word—without later second-guessing—about patient health and public safety.

Respondents and their amici dispute this rule on several fronts, but their arguments fail.

1. Respondents and their amici start with a straw-man: that, on Merck's view, manufacturers may never be liable for failure to warn, because it is the FDA's obligation to "mandate a label change," and so the agency's inaction alone suffices to establish impossibility. Resp. Br. 31–34; *e.g.*, Pub. Citizen Br. 11–12. That theory—essentially, that the enactment of § 355(*o*)(4) in 2007 abrogated *Levine*—is not (and has never been) Merck's argument.

Even after the amendments, the "manufacturer retains the responsibility 'to maintain its label in accordance with existing requirements.'" *Levine*, 555 U.S. at 571 (quoting § 355(*o*)(4)(I)). And, even after the amendments, a court cannot presume that the FDA, with its "limited resources to monitor the 11,000 drugs on the market" and inferior "access to

information" about emerging safety risks, has reviewed the scientific data and passed judgment on the propriety of warning about every possible risk. *Id.* at 578–79. That is why, even after the amendments, the law does not "insulate manufacturers from liability or authorize them to wait to act until mandated by FDA." Resp. Br. 34.

Merck's point is different: Once a manufacturer discharges its duty by bringing a specific risk to the FDA's attention and proposing to warn about it, the agency's denial of that proposal must be understood in light of the duties imposed by the 2007 statutory amendments. The amendments do not change the allocation of duties between manufacturer and regulator. But they do inform our understanding of what it means when the regulator speaks: When an informed regulator formally rejects a proposal to warn of a risk, that ends the matter.

Respondents' amici make a similar error, worrying that, under Merck's rule, the FDA's rejection of a warning means that failure-to-warn claims based on that risk are preempted forever. *E.g.*, Virginia Br. 12. That too is incorrect. If new, material information emerges after the agency's decision, that decision is no longer conclusive; the question under those circumstances would be whether the FDA would have reconsidered in light of that new evidence. But since Respondents point to no new evidence during the relevant period, this case does not present that question.

2. Respondents also contend that § 355(*o*)(4)'s duty is entirely "*discretionary*," so that one cannot infer anything from the FDA's rejection of a proposed warning. Resp. Br. 32. Perhaps the FDA agrees that

the science justifies a new warning but dislikes the manufacturer's phrasing and, exercising its supposed discretion, declines to start a discussion with the manufacturer. If so, Respondents say, then federal law would not have precluded the manufacturer from adding a different warning satisfactory to the FDA.

Respondents' premise is wrong. The word "shall" does not mean "may." To the contrary, the "word 'shall' usually creates a mandate, not a liberty." *Murphy v. Smith*, 138 S. Ct. 784, 787 (2018). So, when § 355(*o*)(4) says that the FDA "shall" initiate a process to modify the labeling when it learns of new information that it believes should be added to the label, it imposes a "nondiscretionary duty" to start that process upon receiving the information. *Id.* The FDA's failure to initiate that process therefore necessarily implies the lack of information that, in its view, justifies a warning.

Respondents' lone citation—*United States v. George S. Bush & Co.*, 310 U.S. 371 (1940)—does not support their unnatural reading of "shall." There, the Tariff Act of 1930 provided that the President "shall by proclamation approve the rates" recommended by the Tariff Commission "*if in his judgment* such rates ... are shown ... to be necessary." *Id.* at 376–77 (emphasis added). The Court held that the statute, by instructing the President to exercise "his judgment" in deciding if a tariff is "necessary," left him with discretion over how to determine necessity. *See id.* at 379–80. The Court never considered the meaning of "shall"—and certainly never hinted that "shall" means "may," so that the President could decline to approve a recommended tariff even after finding it "necessary."

To be sure, § 355(*o*)(4) directs the FDA to begin a label-changing process only if the FDA "determines" that the new information "should be included in the labeling." But it is precisely the FDA's judgment and belief that controls the preemption inquiry, because adding a warning is legally impossible unless the FDA agrees to it. If the agency declines to initiate a § 355(*o*)(4) process, that means it does not believe the new information justifies a new warning—and *that* clearly demonstrates the impossibility of adding such a warning.

3. Respondents and their amici next point out that, long before the plaintiff in *Levine* was injured, the FDA rejected a proposal by Wyeth to change its label on intravenous injection. *See* Resp. Br. 38; Tort Law Professors Br. 21–23; MedShadow Found. Br. 21. If Merck were right, their argument seems to go, then *Levine* should have come out the other way.

Of course, Congress passed § 355(*o*)(4) "after Levine's injury and lawsuit." 555 U.S. at 567. So, *Levine* properly did not consider its effect when deciding what to make of the FDA's decade-earlier decision to reject Wyeth's proposal. *Levine* would have been a poor case in which to address the effect of a previous denial anyway. The majority there found that Wyeth's proposal—which came *twelve years* before Levine's injury, and thus assuredly did not reflect all the available evidence as of the latter date—"did not differ in any material respect from the FDA-approved warning" that was inadequate. 555 U.S. at 572 n.5. Hence the Court's conclusion that the FDA had never "made an affirmative decision" on the central issue. *Id.* at 573.

4. Finally, one of Respondents' amici objects that the FDA's rejection of Merck's proposal is mere "agency action," which (unlike "laws" and "treaties") carries no preeemptive force under the Supremacy Clause. Cato Inst. Br. 1. That misses the point. It is not *the FDA's rejection* that preempts Respondents' claims. It is *§ 355*—undeniably among the "laws of the United States"—which prohibits the sale of drugs without an FDA-approved label. The FDA's rejection matters only because it proves the impossibility of issuing an FDA-approved label that includes the state-mandated warning. "Many other federal statutes preempt state law" in similar fashion, and this Court unanimously upheld one against an identical Supremacy Clause challenge just two terms ago. *Coventry Health Care of Mo., Inc. v. Nevils*, 137 S. Ct. 1190, 1198 (2017); *id.* at 1199 (Thomas, J., concurring) (writing separately to note that such laws must constrain executive discretion to avoid improper delegation).

B. This Legal Rule Preempts Respondents' Claims Here.

Under this legal rule, Respondents' claims are preempted. There is no dispute on the three key predicates. *First*, Merck "kept the FDA informed" of "scores of case studies, reports, and articles ... documenting possible," albeit uncertain, "connections between long-term bisphosphonate use and atypical femoral fractures." Pet.App.13a; *see also* Pet.App.13a–14a. *Second*, after the FDA told Merck that it was "concerned about this developing safety signal," Pet.App.14a, Merck proposed a Precaution to "address atypical femoral fractures," Pet.App.15a—that is, addressed to "[l]ow-energy fractures of the

subtrochanteric and proximal femoral shaft," J.A.707. *Third*, the FDA rejected that proposal. J.A. 510–13. It follows that it was impossible for Merck to have warned about those fractures before September 2010, when the FDA revisited the issue in light of the intervening task force report.

Respondents object to this application of law to fact in two respects. *First*, they contend that Merck "never proposed a warning of atypical femoral fractures to FDA," because its proposal concerned a (supposedly) different injury—"stress fractures." Resp. Br. 35. *Second*, they argue that the FDA did not *really* reject Merck's proposal. Resp. Br. 40. Neither argument withstands even minimal scrutiny.

1. Respondents insist that because Merck's warning mentioned "stress fractures" several times, Merck sought to warn only about minor injuries suffered by (for example) new joggers, not the atypical femoral fractures that injured Respondents. Resp. Br. 36–38. This Court presumably rejected that revisionist history in granting certiorari. *See* BIO 18–19. It should do so again.

No one could reasonably believe that Merck was trying to warn about anything besides the type of injuries that Respondents suffered—or that the FDA was confused about that. Take first the proposed label itself. Its *title* addressed "low-energy femoral shaft fracture[s]." J.A.707 (capitalization altered). Its first sentence reiterated that focus, addressing "[l]ow-energy fractures of the subtrochanteric and proximal femoral shaft," *id.*—the definition of atypical femoral fractures, not just a name.

The rest of Merck's proposed label followed suit. As Respondents' expert and amici note, atypical femoral fractures have two distinctive characteristics: they are "insufficiency" fractures (meaning they occur with normal activity on bones of abnormally decreased density), and they often progress to "complete" fracture (meaning the bone is split all the way through). *E.g.*, J.A.100, 136; Lane Br. 9–10, 18. Merck's proposed label identified both of those characteristics: some of the "insufficiency fractures" in question had progressed to "complete fracture." J.A.707. And the rest of Merck's application further made clear that Merck was talking about atypical femoral fractures. *E.g.*, J.A.748 (noting reports of "low-energy subtrochanteric / mid femoral shaft fractures"); J.A.753 (noting that, of 65 reports that included "information on fracture management," the six patients with "incomplete" fractures were "treated conservatively" while the 59 others had "surg[ery]"); J.A.746 (noting that some of these "insufficiency" fractures were caused by "normal" activity). Given these materials, it defies belief to think that Merck was talking about something categorically different when it proposed its warning.

To be sure, the proper terminology for these fractures was unsettled in 2008, but they were often referred to as stress or insufficiency fractures. *Compare, e.g.*, S.K. Goh et al., *Subtrochanteric Insufficiency Fractures in Patients on Alendronate Therapy*, 89 J. Bone & Joint Surgery 349 (2007) (cited in the FDA's request for additional information, J.A.281), *with* E.B. Kwek et al., *An Emerging Pattern of Subtrochanteric Stress*

Fractures: A Long-Term Complication of Alendronate Therapy?, Injury, Feb. 2008, at 224–231. Indeed, the very expert task force with whom the FDA worked to evaluate the issue confirmed that atypical fractures "*are* stress fractures" whose ordinary healing may be interrupted by the "suppression of remodeling" that is associated with long-term bisphosphonate use. Elizabeth Shane et al., *Atypical Subtrochanteric and Diaphyseal Femoral Fractures: Second Report of a Task Force of the American Society for Bone and Mineral Research*, 29 J. Bone & Min. Res. 1, 12 (2014) (emphasis added). At a bare minimum, even Respondents' expert and amici concede that atypical femoral fractures "start as ... stress fracture[s]." Lane Br. 12; *e.g.*, J.A.145 (claiming that Fosamax "allow[s] the initial stress fracture lesion to continue to grow until complete fracture").

In any event, the way Merck used this term was clear from the face of its application, as Merck explained that choice in its proposal. *See, e.g.*, J.A.670 ("Merck is proposing to add language ... to describe low-energy fractures that have been reported, of which some have been stress/insufficiency fractures"). While the FDA ultimately concluded (among other things) that Merck's discussion of stress fractures might cause confusion, it always recognized—indeed, it has affirmatively stated—that Merck tried to warn about atypical femoral fractures. *See* U.S. Br. 30 (the "exact same risk"). In short, whatever the merits of Merck's terminology, everyone knew what it was talking about—especially the FDA.

Respondents note that the "FDA and Merck have acknowledged the crucial distinction between stress

fractures and atypical femoral fractures," and point to a (later) 2010 exchange during which the FDA removed a reference to "stress fractures" from Merck's suggested revisions to the FDA's proposal. Resp. Br. 36; *see* J.A.566. This proves *Merck's* point: Merck's terminology did not confuse the FDA; rather, the FDA understood precisely the risk that Merck was seeking to warn about.

Finally, Respondents object that Merck's proposed warning "obscured the nature of atypical femoral fractures," by failing to explain "the scientific mechanism" by which Fosamax causes them, and by noting that similar fractures had also occurred prior to the availability of bisphosphonates. Resp. Br. 37–38. Neither point has any legal relevance, since (as explained) there is no claim that Merck concealed any material information from the FDA, and no plausible concern that the FDA misunderstood the nature of the risk at issue. Regardless, both of Respondents' complaints fail on their own terms. The scientific process by which Fosamax may contribute to atypical femoral fractures had been well-documented in "scores of case studies, reports, and articles" dating back years, Pet.App.13a, and Merck's PAS cited those at length, J.A.748–49. And while these types of fractures are "*predominantly* seen in bisphosphonate users," Resp. Br. 37–38 (emphasis added), Respondents' qualifier gives away the game. To this day, Fosamax's FDA-approved label informs doctors that "these fractures also occur in osteoporotic patients who have not been treated with bisphosphonates"—because they do. J.A.223. In neither respect did Merck mislead the FDA at all, much less in a legally material way.

2. Despite conceding in the Third Circuit that the FDA's rejection of Merck's proposal was "final, written regulatory action[]," Resp. CA3 Letter, at 3, Respondents now insist that the FDA did not *really* reject Merck's proposal. Pointing out that the FDA's complete response letter told Merck that it was free to "resubmit" the application if it did not wish to withdraw it, Respondents argue that Merck could have resubmitted a revised warning by filing a new PAS or through the CBE process. Resp. Br. 40; *see also* Pub. Law Scholars Br. 17–18.

Of course it is true that Merck had the technical right to refile its proposal or to engage the CBE process, and the FDA acknowledged as much in boilerplate language. But that hardly matters if the FDA would have rejected a resubmitted warning. As explained above, it clearly would have. The statute and the FDA's own regulations required the agency to take specific steps if it determined that a warning was warranted. Its failure to do so thus shows its determination that a warning was *not* warranted at that time, based on the complete scientific data that Merck provided to it. And that determination, in turn, makes plain that the FDA would not have suddenly turned around and approved a resubmitted warning about the same risk, based on the same data—whether Merck sought permission (under the PAS process) or forgiveness (under the CBE process). Indulging in Respondents' contrary speculation would make it impossible *ever* to prove impossibility preemption. *See PLIVA, Inc. v. Mensing*, 564 U.S. 604, 623 (2011) (plurality op.) (warning against denying preemption based on "speculation").

II. MERCK PREVAILS IN THIS CASE UNDER ANY LEGAL FRAMEWORK.

The rule set forth above, focused on the meaning and effect of the FDA's actual decision, provides the cleanest way to resolve this case and provide helpful guidance in this confused area of the law. But even without that rule, Respondents' claims are still preempted. The FDA has now unambiguously told this Court that it rejected Merck's proposal on scientific grounds and therefore would not have approved *any* warning about atypical femoral fractures before the task force published its report in September 2010. That dispositive representation simply corroborates what the undisputed record already showed, despite Respondents' distractions. Indeed, the Third Circuit overcame the force of that record only by adopting a clear-and-convincing standard of proof that Respondents only half-heartedly defend.

A. The FDA Has Told This Court That It Would Not Have Approved a Warning.

Everyone agrees that Merck wins if it has "clear evidence that the FDA would not have approved" the warning supposedly required by state law. *Levine*, 555 U.S. at 571; *see* Resp. Br. 30. Even if the denial of Merck's proposal, standing alone, does not satisfy that test as a matter of law, other evidence does.

The United States has stated that the FDA "rejected a change to Fosamax's Warnings and Precautions because the data at that time was insufficient to justify a change." U.S. Br. 30 (capitalization altered). "It was only in October 2010—after an external task force had completed its

report on the issue—that FDA came to 'believe that the information' about atypical femoral fractures should be added to the Warnings and Precautions section." *Id.* at 33 (quoting J.A.527–28). It is hard to get clearer evidence than that.

Respondents insist, however, that these statements are merely "legal argument" from the Office of the Solicitor General. Resp. Br. 45. They then insist that the United States' views deserve no weight because "no regulation purportedly preempts state law" and because of growing skepticism about *Auer* deference. *Id.* at 45–46.

Wrong on both fronts. Respondents' first complaint seems to be that the United States' brief does not expressly state that the FDA agrees with its statements about Fosamax's regulatory history. But the United States' brief *is signed by* the FDA's parent agency, the Department of Health and Human Services. Respondents cannot seriously contend that the brief's statements about how the FDA operates and about how the FDA discharged its duties in acting on Merck's application do not reflect the FDA's views or representations.

Moreover, even if the United States' brief merely reflected the FDA's "legal argument" about its own actions, it still must "make a difference" in the preemption analysis. *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 883 (2000). Respondents concede that, had the FDA promulgated a *regulation* and explained its purposes (as in *Geier*), the FDA's views would be given "weight" in determining whether state law stands as an obstacle to federal law. Resp. Br. 45. They fail to explain why a much less problematic agency "interpretation"—its explanation

of why it rejected Merck's proposal and its view of the science at the time—deserves no weight in determining whether *the agency itself* "would not have approved" a change to Fosamax's label. *Levine*, 555 U.S. at 571. Who better to explain the FDA's actions than the FDA?

For similar reasons, the "equal protection concerns" arising from "regulat[ion] by *amicus* brief," Resp. Br. 46, are absent here. The United States' brief—which tracks its certiorari-stage amicus brief, filed upon invitation from the Court—is not an attempt at regulation, merely an explanation of FDA action. Accepting its explanation would not make it harder for "people to know if their conduct is permissible when they act." *E.I. du Pont de Nemours & Co. v. Smiley*, 138 S. Ct. 2563, 2564 (2018) (Gorsuch, J., respecting the denial of certiorari). Nor would it "incentiviz[e] agencies" to promulgate ambiguous regulations, *id.* at 2564, none of which is at issue here. Whatever the validity or vitality of the *Auer* doctrine, there is no reason to let juries second-guess the FDA's own unequivocal statement about what it would have done with a rephrased warning.

If the question whether the FDA would have denied a warning is to be a question of fact, as Respondents say, then the best available evidence of what the FDA would have done (its own say-so) has to be relevant.

B. Every Other Piece of Evidence Cuts in Merck's Favor as Well

Although the United States' brief is new, its point is hardly novel. Rather, its statements fit neatly with the rest of the record, which already

showed beyond reasonable dispute that the FDA's denial of Merck's proposal was based on more than semantic quibbles. In arguing otherwise, Respondents misread the key document, divorce agency statements from their factual context, and ignore the overwhelming evidence that the agency was not ready to permit any warning until the task force report brought new clarity to the nature of the risk at issue.

Take first the FDA's complete response letter rejecting Merck's proposal. There, the FDA set out its "reasons" for "determin[ing]" it could not grant approval. The first reason? "[Y]our justification for the proposed PRECAUTIONS section language is inadequate." J.A.511.

Respondents insist that the letter "offered only one reason for rejecting" Merck's proposal: that it talked about stress fractures. Resp. Br. 39. Not so. To the extent that the FDA took issue with Merck's references to stress fractures, that was *in addition* to Merck's "inadequate" "justification" for the warning, not an *elaboration* of that inadequacy. After all, FDA provided "*reasons*" for rejecting the PAS—in the plural—not "only one reason." J.A.511.

Next, consider that, at the same time it denied Merck's proposed warning, the FDA also accepted Merck's request to add "low energy femoral shaft *and subtrochanteric* fractures" to the Adverse Reactions sections—with the italicized words differing from Merck's original proposal. J.A.512; *compare* J.A.728. Respondents claim that this shows that the FDA "was willing to approve a warning" but disliked Merck's language. Resp. Br. 41–42. Actually it shows the opposite. The FDA's redline of Merck's

Adverse Reactions proposal—and complete absence of any redlining on Merck's Precautions proposal—confirm that the FDA did not ignore patient safety by rejecting Merck's request for semantic reasons. The disparate treatment of the two proposals flows from the fact that Precautions require a more certain causal association, which the FDA did not believe existed. *See* Merck Br. 9–10.

The agency's conduct before sending the complete response letter drives the point home. A month earlier, an FDA official told Merck to "hold off on the W&P language" so it could "close out these supplements" and then "work with" Merck on a new warning "*if it is warranted.*" J.A.508 (emphasis added). Respondents, omitting the key part of the quote, insist that this document proves the FDA did not "definitive[ly] reject[]" a warning in the complete response letter that followed. Resp. Br. 48. But it did just that: The FDA told Merck it wanted to "*close out*" Merck's PAS, study the issue more, and *then* add a warning "if it is warranted." Respondents have no answer for why the FDA would say such a thing if it already knew enough to accept changes.

Nor can Respondents explain Merck's phone call with the same FDA official who drafted the complete response letter, during which the official told Merck that "[t]he conflicting nature of the literature d[id] not provide a clear path forward, and more time w[ould] be need[ed] for FDA to formulate a formal opinion on the issue of a precaution." J.A.767. Respondents insist that this compelling evidence is "self-serving hearsay." Resp. Br. 47. But they did not object to the record's admission or seek to depose the recordkeeper before the District Court.

The FDA's conduct after the complete response letter also refutes Respondents' story. In March 2010, the FDA told doctors to "continue to follow the recommendations in the [unrevised] label" while it "work[ed] closely with outside experts" "to gather additional information that may provide more insight." J.A.519–20. Respondents fight back against a single line in this document—the FDA cited the lack of a "clear connection" between bisphosphonate use and atypical femoral fractures, but did not deny that there was "reasonable evidence of a causal association," which is the regulatory standard to add a Precaution. Resp. Br. 48–49 n.26. But Respondents do not try to explain why the FDA would have told doctors to *keep prescribing Fosamax as labeled* if it already knew enough to justify a revision.

Finally, whatever doubt might be left at this point vanishes when one considers the events following the task force report. Respondents contend that the FDA's 2010 decision to mandate a warning "confirms that it was possible for Merck to add an adequate warning" earlier. Resp. Br. 48. Again, just the opposite is true. The FDA ultimately chose to mandate a warning *because of* the task force report, which was published only in September 2010. As the Deputy Director of the Office of New Drugs explained, "[b]ased on that report," and particularly its crafting of a provisional case definition, the FDA was "able to better assess some of the cases reported to" it. J.A.488. Indeed, when she was asked "what new data between March and now have you reviewed" to justify a warning, she cited the report,

explaining that it had been "really helpful to [the FDA] in better understanding this." J.A.492–94.

In short, the FDA's refusal to accept (or even to redline) Merck's proposal, along with its insistence that more research was needed before a new warning could be approved, and its ultimate crediting of the task force report for changing its mind, all make it impossible to believe that Merck could have changed its label at any time before September 2010.

C. There Is No Heightened Burden of Proof for Preemption.

The Third Circuit, however, reached a contrary conclusion because it demanded that Merck satisfy a heightened evidentiary burden. Unlike the Third Circuit's speculation about whether a judge or jury should decide what the FDA would have done with a revised warning (which all admit was unnecessary dictum, Resp. Br. 50), the Third Circuit's statements on the burden of proof were essential to its holding: It denied summary judgment solely because, in its view, a reasonable factfinder could find that "the odds of [an] FDA rejection were *less than highly probable*." Pet.App.5a (emphasis added). Respondents' three reasons for imposing such a requirement are unpersuasive.

First, Respondents say that *Levine*'s use of the phrase "clear evidence" is "consistent with a heightened standard of proof." Resp. Br. 56. Maybe so, but it is equally consistent with Merck's reading: that preemption must be based on evidence rather than conjecture. Merck Br. 46; *see, e.g.*, *Block v. Cmty. Nutrition Inst.*, 467 U.S. 340, 350–51 (1984) (using the phrase in this way). And the latter is the

far better reading, because it comports with the general rule that, absent statutory direction, courts do not invent heightened burdens of proof unless fundamental rights are at stake. *See, e.g.*, *Santosky v. Kramer*, 455 U.S. 745, 769–70 (1982) (termination of parental rights); *Addington v. Texas*, 441 U.S. 418, 433 (1979) (involuntary commitment). Respondents do not claim that their mine-run tort suits implicate concerns of that magnitude.

Second, Respondents say a heightened burden is necessary because *Levine* "stretched the bounds of impossibility preemption" by allowing manufacturers to prove preemption even where it is "physically possible" to comply with both state and federal law. Resp. Br. 56. Respondents' premise is wrong: If state law requires a warning that the FDA would prohibit, it is not "physically possible" to issue that warning without violating federal law. And all agree that a manufacturer must make that showing (that is, that the FDA would have prohibited the warning) to prevail on its preemption defense. The question here is by what standard of proof must the manufacturer do so. The difficulty of proving the defense is not a reason to heighten the standard of proof beyond the ordinary preponderance standard that governs all ordinary civil litigation.

Finally, Respondents accuse Merck of conceding that some heightened burden applies, even if it is not quite as high as the clear-and-convincing standard. Resp. Br. 56. That would be irrelevant even if it were true; Respondents feign difficulty imagining "a case that would turn on whether the defense requires proof by clear-and-convincing evidence," Resp. Br. 56–57, but the Third Circuit suggested this

was (in its view) exactly such a case, and that Merck would prevail without the clear-and-convincing standard. Pet.App.62a, 67a.

Anyway, Merck never conceded this. Merck denied that *Levine* imposes a heightened burden, arguing that *Levine*'s "clear evidence" language simply requires courts to base preemption findings on evidence rather than speculation. Merck Br. 46. If the manufacturer produces such evidence, and if it establishes by a preponderance of the evidence that the FDA would have rejected any revised label, then it has carried its burden. Especially given the Supremacy Clause's *non obstante* provision, courts may not distort federal law—for example, by adding a heightened burden—to avoid a conflict with state law. *Mensing*, 564 U.S. at 623 (plurality op.).

III. Respondents' Procedural Complaints Are Meritless and Irrelevant.

Respondents finally argue that the District Court violated due process (or perhaps the Federal Rules of Civil Procedure?) by giving them only 45 days to develop evidence in response to a show-cause order after the bellwether decision in *Glynn*. Resp. Br. 57–58; BIO 29–30 Although this Court need not resolve this complaint—which the Third Circuit never passed upon—the argument is easily rejected.

Respondents had far more than 45 days to gather their evidence. As the District Court explained, they had "been aware of the potential global effects preemption could have on the entire MDL for at least two ... years." Pet.App.124a. Throughout that period—designed to efficiently provide core discovery to all plaintiffs in all cases with respect to common

issues—Respondents "were aware of the exact position that Merck took surrounding preemption," *id.*, and had a full seven months of fact discovery, Pet.App.124a–30a. All of that occurred before *Glynn*'s bellwether trial. Only after that trial, and further briefing on preemption there, did the court order Respondents to show cause, giving them another 45 days to adduce additional evidence. It does not violate due process (or an unspecified rule) to give a party "yet another opportunity ... to address what has *long* been known as the predominant issue in a case." Pet.App.129a–30a.

Nor can Respondents show any real prejudice. They now contend that, with extra time, they would have deposed the Merck employee who took notes during a call with an FDA official. Resp. Br. 58. But Respondents never asked to depose that employee, even though Merck had long pointed to her notes as one piece of evidence in its favor. *See* Dkt. 129, No. 11-cv-05304 (D.N.J.) (*Glynn*). Respondents' remorse over their own procedural missteps is no basis to reverse a grant of summary judgment.

The same goes for Respondents' claim that the "schedule" somehow prevented some of them from arguing that Merck could have issued—and they "would have ... heeded"—a revised warning during the gap between the FDA's rejection of Merck's proposal and the task force's report. Resp. Br. 58 n.32. Manufacturers may amend their labels using the CBE process based only on "newly acquired information." 21 C.F.R. § 314.70(a)(6)(iii). And Respondents never point to any new, material information that emerged after the denial of Merck's proposal (in May 2009) but before the task force

report (in September 2010). Plus, the only evidence Respondents say they would have needed to make this futile point—evidence about "when the warning would have been heeded," Resp. Br. 58 n.32—was exclusively within their own control. It hardly requires more than 45 days to gather *that*.

CONCLUSION

The Court should reverse the judgment below.

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Respectfully submitted,

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